IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

Claims 1-6 (canceled)

7. (currently amended) A method for determining ~~development of RA or the likelihood of developing RA~~ whether a human subject is at increased risk for developing rheumatoid arthritis, comprising: ~~comparing a methylation state of a DR3 gene promoter region obtained from synovial cells or synovial infiltrating lymphocytes with a methylation state of a DR3 gene promoter region obtained from peripheral blood lymphocytes, or confirming that the DR3 gene promoter region obtained from the synovial cells is strongly methylated~~

(i) detecting whether CpG sequences in a region from base 374 to base 592 of SEQ ID NO: 1 in a DR3 gene promoter region obtained from synovial cells or synovial infiltrating lymphocytes of the human subject are methylated or not; and

(ii) determining that the human subject has developed rheumatoid arthritis or has the likelihood of developing rheumatoid arthritis when three or more of the CpG sequences in the region from base 374 to base 592 of SEQ ID NO: 1 are methylated.

8. (currently amended) A method as set forth in Claim 7, ~~further comprising~~ wherein (i) comprises:

a DNA converting step of converting unmethylated cytosines to uracils in CpG sequences contained in the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes~~, and the DR3 gene promoter region obtained from the peripheral blood lymphocytes,~~ by treating the ~~respective~~ DR3 gene promoter ~~regions~~ region with a bisulfite-containing reagent;

a DNA amplifying step of amplifying the DR3 gene promoter ~~regions~~ region, after the treatment in the DNA converting step, by a polymerase chain reaction using methylation-specific primers or unmethylation-specific primers; and

a methylation-state detecting step of detecting ~~a methylation state of the DR3 gene promoter regions~~ how many CpG sequences are methylated, by detecting whether the polymerase chain reaction in the DNA amplifying step using the methylation-specific primers or the unmethylation-specific primers has amplified the DR3 gene promoter ~~regions~~ region~~; and~~

a comparing step of comparing the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes with the DR3 gene promoter region obtained from the peripheral blood lymphocytes, in regard to the methylation state of the DR3 gene promoter A regions detected in the methylation-state detecting step, or a confirming step of confirming that the DR3 promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is strongly methylated.

9. (currently amended) A method for determining whether a human subject has developed rheumatoid arthritis or has a likelihood of developing rheumatoid arthritis, comprising:

detecting whether CpG sequences from base 374 to base 592 of SEQ ID NO: 1 in a DR3 gene promoter region obtained from synovial cells or synovial infiltrating lymphocytes of a human subject are methylated or not;

detecting whether CpG sequences from base 374 to base 592 of SEQ ID NO: 1 in a DR3 gene promoter region obtained from peripheral blood lymphocytes of the human subject are methylated or not;

comparing methylation of the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes with methylation of the DR3 gene promoter region obtained from the peripheral blood lymphocytes; and

determining that the human subject has developed rheumatoid arthritis or has the likelihood of developing rheumatoid arthritis when the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is methylated at higher ratio than the DR3 gene promoter region obtained from the peripheral blood lymphocytes ~~as set forth in Claim 7, wherein the method determines that the subject has developed RA or has the likelihood of developing RA when the DR3 promoter~~

~~region obtained from the synovial cells or synovial infiltrating lymphocytes is more strongly methylated than the DR3 promoter region obtained from the peripheral blood lymphocytes~~.

10. (currently amended) A method for determining whether a human subject has developed rheumatoid arthritis or has a likelihood of developing rheumatoid arthritis, comprising:

detecting whether CpG sequences from base 374 to base 592 of SEQ ID NO: 1 in a DR3 gene promoter region obtained from synovial cells or synovial infiltrating lymphocytes of a human subject are methylated or not;

comparing methylation of the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes with a control that is methylation of the DR3 gene promoter region obtained from peripheral blood lymphocytes of a healthy human subject; and

determining that the human subject has developed rheumatoid arthritis or has the likelihood of developing rheumatoid arthritis when the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is methylated at higher ratio than the DR3 gene promoter region originating in the peripheral blood lymphocytes of the healthy human subject ~~as set forth in Claim 7,~~

~~wherein a DR3 gene originating in the peripheral blood lymphocytes of healthy subjects is used as a control; and~~

~~wherein the method determines that the subject has developed RA or has the likelihood of developing RA when the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is more strongly methylated than the DR3 promoter region originating in the peripheral blood lymphocytes~~.

Claims 11-12 (canceled)

13. (new) A method as set forth in claim 6, wherein the methylation-specific primers and the unmethylation-specific primers are designed to amplify at least the nucleotide sequence from base 374 to base 564 of SEQ ID NO: 1.

14. (new) A method as set forth in claim 8, wherein:

the methylation-specific primers are a primer set specified in SEQ ID NOS: 2 and 3, and

the unmethylation-specific primers are a primer set specified in SEQ ID NOS: 4 and 5.